# External Peer Review

# of the

# Food & Drug Administration's

# Office of Regulatory Affairs Pesticide Program

**Submitted to:**

**FDA Science Board**

**DRAFT**

**September 28, 2005**

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## *Summary of Charge*

Food and Drug Administration's Office of Regional Affairs (ORA) conducted an internal review of their Pesticide Program in 2004 and reported their findings in an October 12, 2004 report entitled "Report of the ORA Science Peer Review Committee on the FDA Pesticides Program." The report contained both Scientific and Program Management recommendations for FDA's Pesticide Program. John Marzilli, FDA Deputy Associate Commissioner for Regulatory Affairs, and John Specchio, Ph.D., Co-chair Science Advisor Division of Field Science, Professor Montclair State University, presented the Report's Science Issue recommendations to FDA Science Board at the November 2004 Meeting. FDA Science Board Chair, Kenneth Shine, MD, named a Peer Review Panel (Panel, Appendix 1) to review the Report and to make recommendations for consideration by the full FDA Science Board.

The Panel was charged to address only the Science Issue recommendations in the ORA Report and to provide additional insight into specific sampling and methods considerations for agrochemical pesticides. This report addresses this charge.

## *Panel Approach*

The Panel visited the State of Florida Bureau of Chemical Residue Laboratories in March 2005, the FDA Headquarters in April, and the FDA Pacific Regional Laboratory Southwest (PRL-SW) in Irvine in May 2005 to enhance exchange of information from a variety of sources and to facilitate development of recommendations. While the focus of this report is on Science Issues, the Panel encountered examples of management issues that influence scientific results. The Panel considered these management issues within the scope of the review.

In this report, the Panel provides observations and recommendations on General Considerations for FDA's pesticide program and specific considerations related to Sampling and Methods. The ORA report included organization and management issues important in the development of a scientifically valid and effective program.

The overall finding of the Panel's review was that clear articulation and definition of goals pertinent of the pesticide program is needed to improve implementation of the program.

## *General Considerations*

The Panel considered the specific Science Issue recommendations in the original ORA report and provided a summary of observations (Appendix 2). It is important to note that FDA's pesticide program is not solely ORA's responsibility. The Center for Food Safety and Nutrition (CFSAN) and the Center for Veterinary Medicine (CVM) also play a role in identifying appropriate samples. Additionally, the Environmental Protection Agency (EPA) sets tolerances and the U.S. Department of Agriculture (USDA) evaluates certain commodities in the U.S. food supply. Because of this there is considerable need for coordination and articulation of goals.

### Observation 1: FDA needs to clearly define goals, requirements, and desired outcomes for its pesticide program.

Agricultural practices in the food supply have changed over the last two decades and FDA's pesticide monitoring programs should reflect public health and safety needs. Factors to consider include:

- Globalization of the food supply
- Changes in pesticide use, such as decreased use of organophosphates and chlorinated hydrocarbons and increased use of new bio-rationally designed pesticides in the U.S.
- Changes in public health
- Consumers' perception of risk

RECOMMENDATIONS:

- Collaboration within FDA and across other agencies to clearly define goals of ORA's pesticide program.
- Implement a more effective information management system for sampling and methods.
- Re-focus available resources to better mirror public health and safety interests.

## *Sampling Considerations*

The ORA report covered three different programs:

- The Total Diet Study evaluates the incident of pesticide levels and other contaminants, and is used by EPA and others for risk assessment.
- The Dioxin sampling monitors incident levels for risk assessment purposes.
- The Regulatory pesticide sampling monitors compliance with EPA tolerances to support regulatory enforcement activities.

Sampling considerations for each of the programs reviewed vary based on their purpose. The regulatory pesticide program is the largest of these and the Panel focused on this program. The total number of samples in this program dropped from a high of about 20,000 samples per year during the 60's and early 90's to about 8000 per year in 2004 for all commodities. This includes both domestic and import samples. There has been an increased emphasis on import products.

There is need for a coordinated strategy for design and implementation of sampling programs. This would include consideration of:

- Potential health risks
- Coordination of sample collection with efficient laboratory scheduling and analysis
- Effective use of other data (e.g., from States) to target sampling in areas and crops where violations are more likely to occur
- Availability of crops due to seasonality, regional growing practices, and import shipments

Collaboration with regions, states, and countries would allow for more effective utilization of resources by avoiding duplication of regional or state efforts. For example, if a commodity showed little or no violation over several seasons in a particular region through continued state surveillance, it would be prudent for FDA to focus resources on other commodities or to compliment the efforts of other state agencies where their data are lacking. This will require a policy change. Sampling plan development could also benefit from harmonization with state sampling programs when they are developed with a strong understanding of growing patterns and crop availability. Done effectively, this could prevent duplication of effort and enhance broader coverage of sampling through a coordinated effort.

### Observation 2: Pesticide sampling should be risk-based.

The Panel did not observe a risk based approach to the regulatory sampling program. Sampling plans provided by CFSAN provide insufficient guidance for efficient coordination of sample collection. For example, the plan may allow for the collection of samples that present a low risk to public health but may have a high violation rate (e.g., arrowroot). In conjunction with regional offices, CFSAN should provide more specificity in the Work Plan to guide sample collection that is based on public health risk.

FDA’s pesticide regulatory program is not intended to supply data to be used for risk assessment, as are data generated by the USDA's Pesticide Data Program (PDP). If such a dual purpose was

intended for FDA data, significant changes would be needed to the sampling and analysis aspects of the program.

FDA's pesticide regulatory program would benefit greatly from a sampling program that targets those commodities posing the greatest risk to food safety. Factors to consider include:

- Commodities that have had violations in the past
- The volume of product imported or grown in the U.S.
- The availability and distribution of a commodity
- The lack of surveillance by other agencies such as the States
- The severity of health risk posed by a suspected violation
- Vulnerable sub-populations
- Currently identified health hazards
- Counter-terrorism priorities

Significant scientific resources would be needed to provide such risk-based sampling guidelines. If provided by FDA and well understood by the scientific community, these risk-based guidelines could be used to improve regulatory programs within and outside FDA.

RECOMMENDATIONS:

- ORA and CFSAN should jointly reevaluate commodities to be sampled using a risk-based approach focused on public health needs and patterns of non-compliance.

### Observation 3: Current pesticide sampling is not statistically based.

Goals must be articulated to apply appropriate statistical sampling to meet those goals. There was no evidence of clear program goals for the pesticide program. For example, the number of samples needed to meet statutory requirements or the number and type of commodities being sampled can be defined if the goals are understood.

The violation rates in FDA's pesticide program have recently been relatively low (2-5%). These low violation rates require large numbers of samples for statistical significance at greater than 95% confidence. Current sample numbers are not high enough to provide this level of statistical significance. In some instances, statistical sampling may not be necessary to reach program goals. For example, if the goal is to detect violative samples, then targeting repeat offenders may be sufficient. However, this may target low consumption foods that may not present a public health risk.

The Panel did not receive sufficient information on the Dioxin or Total Diet studies to evaluate statistical soundness.

RECOMMENDATIONS:

- On-going consultation with statisticians is recommended to meet defined program goals.
- Develop a sampling plan that clearly articulates the data needs of the program.

### Observation 4: There is a general lack of coordination in sample collection and analysis.

The Panel did not observe any method to validate sampling strategies. Sampling plans are issued by CFSAN with little input from ORA. Furthermore there is little coordination among ORA field component districts. While there is a process that provides evidence that the appropriate number of samples has been collected, there does not appear to be a process to ensure that samples collected represent the range of targeted samples. For example, domestic samples are sometimes requested from regions that are not harvesting the specific crop at that time.

The Panel saw varying degrees of coordination used in the collection and timely analysis of samples through effective use of lab and sampling resources and coordination across districts or States. Previously such activities were the responsibility of the Pesticide Coordination Teams identified in the Food Compliance Program for Pesticides and Industrial Chemicals (February 16, 2000). An organized and purpose-driven sampling plan that recognizes lab capabilities together with product seasonality, local availability, growing patterns, and consumption patterns is needed to effectively utilize resources. For example, the Pacific Region uses a web-based Sample Scheduler and weekly conference call to coordinate the number of samples that the lab can receive, which was a useful practice.

RECOMMENDATIONS:

- Enhance coordination efforts between CFSAN, ORA, and other agencies such as the States to select the right samples and the timing of their collection and subsequent analysis.
- Revitalize the Pesticide Coordination Teams particularly for sampling purposes.
- Establish a process that will support efficient use of laboratory resources through notification and scheduled sample submission.
- Interact with the EPA and USDA on supplying data to support risk assessment for sample types (e.g. seafood) for which EPA and USDA do not collect data.

## *Method Considerations*

### Observation 5: The Pesticide Analytical Manual (PAM) is important, and should be updated in a timely manner.

There is an urgent need to update the methods in the PAM as it serves as a repository of officially recognized methods for pesticide residue analysis in foods in the U.S. The PAM currently serves as the national and international standard for pesticide residues in foods. Given the importance of this document, allocation of resources to update the document is essential if it is to remain useful. It is currently not being maintained due to lack of resources and the diminishing focus on pesticides within the FDA.

A clearly defined process for timely incorporation of new methods into the PAM I is needed. The PAM editorial board does not have authority to recommend and approve methods for incorporation into PAM I. Despite evidence that FDA is developing and using new methods, they are not being added to the PAM in a timely manner. Agency scientists believe that, for a new method to be incorporated into the PAM, three labs (state or FDA) need to successfully use the method. At present, the development and acceptance of new methods is a lengthy, undefined and an inefficient process.

RECOMMENDATIONS:

- Review, identify and update the Best Practices in the current PAM I immediately.
- Create a process to get validated methods into the PAM in a timely manner.
- Create an incentive for scientists to enter validated methods into PAM.
- Utilize stakeholders and experts in the field for editorial support.

### Observation 6: There should be a defined process for method validation and acceptance.

When newer methods with superior “fit-for-purpose” become available, ORA and FDA should have a process for validation and implementation. Such a process for the development of newer methods and their validation is woefully inadequate within FDA. Furthermore, there is no incentive for FDA scientists to incorporate methods into the PAM. Finally, no formal process is available for evaluating and implementing new methods into laboratory operations.

Methods used for official analyses need to be validated. FDA needs to define a validation process for methods used for official analysis. AOAC, CODEX, ISO and other international organizations have guidelines for varying levels of validation, which may be useful to consider. It should be recognized that in emergency situations, there is need for a process to respond without the benefit of extensive validation. Every effort should be made to provide as much performance and validation information as possible in these situations.

FDA labs sometimes use Laboratory Information Bulletin (LIB) methods for official regulatory samples. This may not be appropriate if the method is not validated. FDA's LIB is a fast way to communicate methods to the field, but they are not peer reviewed or validated. An alternative approach would be to submit methods to a peer-reviewed journal. Similarly, the method could be posted on FDA's website for broader viewing. Some Panel members would like to do away with LIBs because they are not peer reviewed. Others find them to be useful because of the speed with which they can be disseminated and the utility of information in enhancing their own method development.

RECOMMENDATIONS:

- Define a formal process for method validation.
- Use validated methods for official regulatory samples.
- Define a process for use of methods in emergency situations.

### Observation 7: Most methods used to analyze samples are generally cost-effective and efficient, but not comprehensive.

Generally, pesticide methodologies are mature. Nevertheless methodology needs to keep pace with new chemical classes of pesticides. There is a need for more efficient methods capable of analyzing more samples and providing a higher degree of identification and confirmation.

Pesticide methodology could be more cost-effective. Certain materials used in the FDA procedures are expensive and require some custom-made materials that are not commercially available. A benefit to the agency would be to use commercially available materials, implement changes, and streamline the methodology to be inexpensive and efficient.

It is important for methods used in FDA's regulatory program to be selective, sensitive and reproducible enough to identify violations of current pesticide tolerances. As EPA continues to reduce tolerances and register new pesticides, regulatory methods must continually improve to meet these challenges. The regulatory program methods need to analyze an increasingly broader range of pesticides including methods for new classes of pesticides. Also, increasingly more sensitive methods for certain pesticides may be desirable for the Total Diet Study program.

RECOMMENDATIONS:

- Continue to develop a process to harmonize methodology internationally.
- Current FDA methods need to be reevaluated by investigating alternative procedures that may potentially be more cost-effective, faster, and efficient.
- Complete adoption/implementation of using an inexpensive, fast, and efficient multi-residue procedure to all labs.
- Expand screening to Liquid Chromatography/Mass Spectrometry (LC/MS) instrumentation to assay broader classes of pesticides. Immediate cross-utilization of LC/MS within ORA programs can accomplish this goal.
- Define criteria for confirmation and quantitation of pesticides similar to procedures developed by the European Union for veterinary drugs and the State of Florida for pesticides in foods.

## *Other Laboratory Considerations*

### Observation 8: Additional confirmation testing on "no-tolerance pesticides" increases time and resource requirements.

"No tolerance pesticides" are pesticides which have not been registered on specific crops. The establishment of a tolerance requires considerable expense, which is frequently not pursued for low volume food products. Therefore, the absence of a tolerance does not necessarily indicate that presence of a residue represents a significant concern to public health. Nevertheless, presence would constitute a regulatory violation. Due to the lack of sample collection coordination and planning cited above, the laboratories frequently receive commodities that do not have pesticides registered for them.

CFSAN requires an original quantitation and a confirmatory analysis prior to taking regulatory action on samples with pesticide residues for which a tolerance has not been established[1]. Since there is no tolerance all that is necessary is to show that the pesticide is present above the limit of quantitation. The routine procedure followed by the FDA labs has been to run a screening analysis plus the required quantitative and confirmatory analysis (*see Appendix 3 for a detailed description of the process employed by the PRL-SW lab*). In the past, the screening analysis was a rough estimate. Now all the FDA field labs have sophisticated gas chromatographs with mass spectrometers (GC/MS) that are capable of identifying and quantitating pesticide residues. The FDA field labs have demonstrated that by using the GC/MS instruments for screening, the identity and amount of the pesticide can accurately be determined. Pesticide experts in the field would therefore like to use this screening as the confirmatory analysis. This should be sufficient for regulatory action because the criteria for analytical packages state "quantitation of the residue in the confirmatory analysis is not required".

The panel recognizes the savings in resources that would result from this recommendation; however, they emphasize that the labs should provide quantitation results from two separate extractions and that the GC/MS instruments are calibrated regularly.

RECOMMENDATIONS:

- Update the Criteria for Analytical Packages to Support Regulatory Action on pesticide residues, including "no tolerance pesticides" to keep pace with new technology.

### Observation 9: Uniform procedures for capturing, sharing, reporting, and auditing raw data are lacking.

There are no uniform procedures for capturing, sharing, and auditing raw data. Use of electronic data management would be useful. Currently, every report is unique in format, which makes interpretation of results, as well as creating the report more time consuming than necessary. Implementation of a Laboratory Information Management System (LIMS) and archival system would likely create efficiency and allow greater sample throughput. These systems are commercially available and are in use in the private sector. It will also assist with achievement of International Standards Organization (ISO) accreditation.

Raw data should remain with the lab generating the data. In some situations, raw data have been sent to the district. This should be discouraged. Implementation of a LIMS system would enhance availability of the data.

Quantitation and managerial review are the rate limiting steps for dissemination of data. Removal of repetitive quantitation would allow the laboratory to significantly reduce the time it takes to complete analytical packages. Additionally, commercially available LIMS may meet the needs for automatic assembly of reports and archiving of data throughout ORA.

[1] ORA Division of Field Science, Criteria for Analytical Packages to Support Regulatory Action of Pesticide Residues, June 6, 2001.

RECOMMENDATIONS:

- Implement a more effective information management system.
- ORA should evaluate commercially available LIMS that are in use by industry and others to identify and implement a LIMS and data archival system for use by all ORA labs, ORA headquarters and other interested parties (CFSAN).
- The system adopted should automatically generate reports, avoiding the time consuming, manual assembly of information that currently exists.
- Development of individual stand alone systems by components within ORA is not encouraged because an ORA-wide system is required.

### Observation 10: Quality assurance programs are inconsistent across ORA laboratories.

There is an effort to evaluate inter-laboratory methods, but they do not appear to be effective or adopted. Improvement has been observed in analytical methods. Quality Assurance Policies and Procedures were not observed by the Panel. Each laboratory may be at a different level of maturity in development of their Quality Management Program. As laboratories become ISO accredited, these systems will be required and uniform.

RECOMMENDATIONS:

- Complete ISO accreditation.
- Collaborate across laboratories on Quality Assurance Policies and Procedures to maximize consistency of approach and effective utilization of resources.
- Introduce or augment statistically based quality control measures to reduce unnecessary repetition in assaying (e.g. screen vs. original vs. check analysis vs. confirmation).

## *Summary*

At the request of FDA Science Board Chair, Kenneth Shine, the External Peer Review Panel reviewed the Office of Regulatory Affairs Report on FDA's Pesticides Program. The panel also observed laboratory practices and procedures in the State of Florida Bureau of Chemical Residue Laboratories and the FDA Pacific Regional Laboratory – Southwest. A summary of the Panel's observations and recommendations on FDA's Pesticide Program follows.

**Observation 1: FDA needs to clearly define goals, requirements, and desired outcomes for its pesticide program.**

RECOMMENDATIONS:

- Collaboration within FDA and across other agencies to clearly define goals of ORA's pesticide program.
- Implement a more effective information management system for sampling and methods.
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**Observation 2: Pesticide sampling should be risk-based.**

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## *Appendix 1. Panel Members and Participants*

*Panel Members*
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## *Appendix 2. ORA Recommendations and Panel Observations*

| ORA Internal Report (Oct 12, 2004) Science Issues Recommendations* | Panel Observations (2005) |
|---|---|
| *Direction and Leadership*<br>1. Establish a Pesticide Steering Committee (PSC) to address national program issues.<br>2. Create a National Pesticide Expert within ORA. | The Panel agrees that direction and leadership is needed in FDA's pesticide program that focuses on scientific aspects such as consistency and validity of methodology, instrumentation, training, etc. The Panel encourages a formal collaborative approach to address scientific issues. A collaborative approach best supports scientific goals and should extend beyond ORA to include other FDA components such as CFSAN and CVM, as well as other stakeholders such as states, EPA, and USDA. A National Pesticide Expert, if created, needs to have the authority to ensure that recommendations are followed. |
| *Methods*<br>3. The PSC must facilitate continued incorporation of state-of-the-art pesticide methodology into official regulatory procedures. | The Panel agrees that FDA should facilitate continued incorporation of new and fit-for-purpose methods and technologies that are effective, efficient and reproducible into official regulatory procedures for pesticides in a timely manner. Additional observations related to methods are discussed in a separate section. |
| *Policy*<br>4. Establish procedures for retention of analytical records in the analyzing laboratory; establish the Field Accomplishment and Compliance Tracking System (FACTS) sample summary as the official regulatory analytical record.<br><br>5. Review requirements in the Compliance Policy Guides (CPG) for quantitation requirements and check analyses for samples containing "no tolerance" pesticides, as well as pesticides with a tolerance. | Improved procedures for secure storage, retention, and efficient retrieval of original analytical records are recommended for maintaining scientific integrity of the data. The Panel does not believe it appropriate to address specific requirements. Additional considerations are addressed in Observation 9.<br>From a scientific stand point, use of a validated method for screening followed by another confirmatory procedure is sufficient to identify "no tolerance" violations. Validation information must include measures of uncertainty to allow its use for regulatory purposes. Additional considerations are addressed in Observation 8. |

| ORA Internal Report (Oct 12, 2004) Science Issues Recommendations* | Panel Observations (2005) |
|---|---|
| *Domestic and Import Sample Analysis*<br>6. Consolidate all domestic pesticide analyses within two laboratories: Arkansas Regional Laboratory (ARL) for food samples and Kansas City District Laboratory (KN) for feed samples.<br>7. Consolidate all import pesticide analyses in four laboratories: Northeast Regional Lab (NRL), Southeast Regional Lab (SRL), Pacific Regional Lab Southwest (PRL-SW), and Pacific Regional Lab Northwest (PRL-NW). Shift existing import work load from ARL to PRL-SW. | The Panel believes that identification of the specific location for analysis is a management issue outside the scope of this review. However, it is important that analysis be distributed in such a manner that samples are run efficiently and in a timely manner to avoid degradation of residues. |
| 8. Develop a national sampling plan for domestic produce targeting specific commodities for coverage each year and focusing collections to a limited time period.<br>9. Reinitiate statistical sampling surveys to include import products collected in domestic commerce.<br>10. Focus the program in consultation with EPA to provide risk analysis data needed for tolerance reassessment. | The Panel strongly encourages an organized and purpose-driven sampling plan that recognizes seasonality, local product availability, growing patterns, and consumption patterns. This would allow more effective utilization of resources. |
| *Instrumentation*<br>11. PSC should determine configurations of equipment to be used in all pesticide laboratories, utilizing group purchases, whenever appropriate.<br>12. Negotiate and fund service contracts for complex instrumentation.<br>13. The PSC, in development of national protocols, should maximize automation capabilities of instruments. | Items 11-13 are management issues.<br>Standardization of equipment could be beneficial in some instances where routine analysis is conducted. Instrumentation for pesticides is complex and routine maintenance is essential for reliability. ORA management must determine the most cost effective way to manage these issues. |

| ORA Internal Report (Oct 12, 2004) Science Issues Recommendations* | Panel Observations (2005) |
|---|---|
| *Pesticide Analytical Manual (PAM)*<br>14. Initiate a fast-track process for updating PAM I with methods and techniques currently used in FDA laboratories.<br>15. Refocus PAM I as a methods manual, eliminating textbook chapters on general technologies.<br>16. Establish critical limits for adjusting operating parameters when focusing on individual pesticides.<br>17. Establish a schedule for routine updates of both PAM volumes. | The Panel endorses the updating of PAM. PAM is a reference source for states and other countries. Future revisions of PAM could consider international harmonization.<br>There is no organized process for scientists to submit revisions to PAM. This should be established. Additional considerations are addressed in Observation 6. |
| Dioxin Program<br>18. Establish a research effort for dioxin method development at ARL.<br>19. Reaffirm the need for a second dioxin analytical lab at KAN and equip the laboratory appropriately with state-of-the-art technology. | The Panel believes that location of research and analysis programs is a management decision. There are a number of emerging issues that warrant investigations and FDA should prioritize resources based on public health need. The Panel believes that dioxin resources could be used in multiple areas of current interest. |
| *Total Diet Study (TDS)*<br>20. Implement the GC-MSD method in the TDS. | The Panel believes that appropriate technologies should be utilized and addressed this in more detail in the methods section. |
| *Science Dispute Resolution*<br>21. Create and utilize Science Dispute Resolution process based on the ad-hoc procedures described in Regulatory Procedures Manual (RPM) Chapter 10 | The Panel agrees that there should be a process to resolve scientific disputes. |

*The original recommendations were discussed on pages 33 – 43 and summarized on pages 56 – 63 of the ORA report dated October 12, 2004 report.

## *Appendix 3. Pacific Regional Laboratory Southwest (PRLSW) Procedure for No Tolerance Pesticides*

1. Each day a system suitability mix of halogen standards in a matrix blank is run on every instrument to be used for screening. This process establishes a single level external standard calibration. This ensures that the instrument finds and correctly quantitates all the recovered standards comparing them to the Library. *Note: The Library that PRLSW uses for screening is not a NIST or Agilent packaged library but is a library individually created for each instrument by actually injecting 15 mixes of halogen, nitrogen and phosphorus pesticides into that instrument.*

2. A QA recovery of triphenyl phosphate (TPP) is introduced into the solvent prior to sample extraction with every high moisture sample as part of the screening. *Note: High moisture samples account for more than 95% of the samples analyzed by the PRLSW.*

3. Samples are processed through the method and are screened for pesticides. The screening process identifies residues based on the retention time and a spectral match. The amount of pesticide is quantified based on the single level external standard. *Note: Quantitation against the Lab's single level external standard during the screen has been demonstrated to agree well with the standard addition results.*

4. If there is no tolerance set for the pesticide residue on a specific commodity, the residue is quantified by a standard addition procedure (*Note: The lab uses the term "Original Analysis" for this quantitation*). Three standard additions of the detected pesticide are prepared using the same extract analyzed with the screen. When the lab quantitates by standard addition to the matrix for a non-tolerance residue sample, they are essentially showing how the residue behaves in the matrix (*i.e. the standard and the incurred residue have the same retention time and their spectra match each other*). This resembles a recovery in those aspects. A blank is also analyzed concurrently with the standard additions.

5. A confirmatory "check analysis" is also performed. A new extraction is prepared for the confirmatory analysis by a different analyst on a different instrument. For no-tolerance residues, the pesticide is not quantified in the report; however the GC/MSD data can report the amount present. The residue is determined by retention time and the spectral match with an injected standard.

## *Appendix 4. Materials Considered by Panel*

Compliance Policy Guide: Sec. 575.100 Pesticide Residues in Food and Feed - Enforcement Criteria (CPG 7141.01), http://www.fda.gov/ora/compliance_ref/cpg/cpgfod/cpg575-100.html

FDA Compliance Program Guidance Manual, http://intranet.ora.fda.gov/directives/cpgm/master_list.htm

- FDA Compliance Program: 7304.004, Pesticides and Industrial Chemicals in Domestic Foods, (FY '00-02), http://www.cfsan.fda.gov/~comm/cp04004.html
- FDA Compliance Program: 7304.016, Pesticides and Industrial Chemicals in Imported Foods (FY 00/01/02), http://www.cfsan.fda.gov/~comm/cp04016.html
- FDA Compliance Program: 7304.839, Total Diet Studies (FY 03/04/05), http://www.cfsan.fda.gov/~comm/cp04839.html

FDA Pesticide Program, Residue Monitoring, 1993-2003, http://www.cfsan.fda.gov/~dms/pesrpts.html

Investigations Operations Manual 2005, http://www.fda.gov/ora/inspect_ref/iom/

- Investigations Operations Manual 2005, Sample Schedule 3 - PESTICIDE SAMPLES, http://www.fda.gov/ora/inspect_ref/iom/ChapterText/sschedule3.html

ORA Field Management Directives, http://www.fda.gov/ora/inspect_ref/fmd/default.htm

- ORA Field Management Directive No. 129: Interagency Pesticide Referrals Between EPA and FDA, 12/16/92 Revised, http://www.fda.gov/ora/inspect_ref/fmd/fmd129.htm
- ORA Field Management Directive No. 134: Pesticide Coordination Teams, 6/30/94 Revised, http://www.fda.gov/ora/inspect_ref/fmd/fmd134.htm

ORA Laboratory Manual 2004, http://www.fda.gov/ora/science_ref/lm/default.htm

- ORA Laboratory Manual 2004: Section 5 Pesticides Analysis, http://www.fda.gov/ora/science_ref/lm/vol4/section/05.pdf

Pesticide Analytical Manual (PAM), http://vm.cfsan.fda.gov/~frf/pami1.html [links to Volumes I and II]

Pesticides, Metals, Chemical Contaminants & Natural Toxins, CFSAN documents available on the internet, http://www.cfsan.fda.gov/~lrd/pestadd.html

Regulatory Procedures Manual March 2004, http://www.fda.gov/ora/compliance_ref/rpm/default.htm

Southwest Region, Kansas City District, Total Diet and Pesticide Research Center, http://www.fda.gov/ora/science_ref/tdprc/tdprc.htm

Title III - Food Quality Protection Act, SEC. 301. Data Collection Activities to Assure the Health of Infants and Children, http://www.fda.gov/opacom/laws/foodqual/fqpa3.htm

Total Diet Study, http://www.cfsan.fda.gov/~comm/tds-toc.html

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